REMARKS

Claims 1-43 and 57-68 constitute the pending claims in the present application, prior to Amendment. Claims 43, 57-60, 62-66, and 68 are currently under consideration as directed to an elected invention and species. Applicants cancel, without prejudice, claims 1-42 which were previously withdrawn from consideration as directed to a nonelected invention. Applicants reserve the right to prosecute claims of similar or differing scope in future applications. Additionally, Application cancel, without prejudice, claims 57, 59, and 62-68. Cancellation of these claims is not in acquiescence to any of the rejections raised during prosecution of the instant application. Claims 57, 59, and 62-63 are cancelled to avoid redundancy in view of Applicants' amendment to claim 43. Claims 64-68 are cancelled to expedite prosecution. Applicants expressly reserve the right to prosecute claims of similar or differing scope.

Claim 43 has been amended to improve the clarity of the claims and to more particularly point out that the compound for use in the claimed method is a "Sonic hedgehog blocking antibody". Support for Applicants' amendment can be found, for example, in paragraphs [0029], [0089], and Example 4 of the published specification. Further support for the use of the claimed compounds in methods of inhibiting vascular growth can be found, for example, in paragraphs [0060], [0096], [0107], and [0118] of the published specification. Further support for the use of the claimed compounds can be found, for example, in paragraphs [0078], [0089], [0093], and [0095] of the published specification.

Claim 58 has been amended to improve the clarity of the claims and to more particularly point out that the Sonic hedgehog blocking antibody inhibits angiogenesis. Support for Applicants' amendment can be found, for example, in paragraph [0042] of the published specification. Applicants' amendment is not believed to narrow the scope of the claim but, rather, is believed to improve the clarity of the claim.

Claims 60 has been amended to improve the clarity of the claims by deleting recitation of "enhanced vascular growth accompanies a solid tumor." Applicants' amendment is not believed to narrow the scope of the claim but, rather, is believed to improve the clarity of the claim. Applicants note that, although claim 61 is directed to a nonelected species, Applicants have made a conforming amendment to claim 61. Applicants' amendment is not believed to narrow the scope of the claim but, rather, is believed to improve the clarity of the claim.

Applicants add new claims 69-74. Support for the subject matter of claims 69-74 can be found, for example, in paragraph [0118] of the published specification. Further support can be found, for example, in paragraphs [0029], [0060], [0078], [0089], [0093], [0095], [0096], [0107], and Example 4 of the published specification. The cited passages provide explicit support for the use of the claimed compounds in methods of inhibiting vascular growth. No new matter has been entered. Claims 69-72 read on the elected invention and species.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below. Applicants will first address the issue raised in the Advisory Action mailed May 20, 2008. Applicants will then reiterate for the record the arguments advanced in response to the Office Action mailed January 8, 2008.

Issue Raised in the Advisory Action

In the Advisory Action mailed May 20, 2008, the Examiner refused to enter Applicants after-final amendments because Applicants' amendments allegedly raise the issue of new matter. Applicants traverse.

The Examiner cited *Purdue Pharma v. Faulding* and *In re Ruschig* as allegedly supporting the New Matter Rejection. However, the Examiner's reliance on these cases is misplaced because the factual situation underlying these cases is distinct from that present in the instant application. These factual distinctions are critical to any written description analysis, as was appreciated when the court in *Purdue Pharma* reiterated the maxim that compliance with the written description requirement is a factual inquiry that "must be assessed on a case-by-case basis." *Purdue Pharma L.P v. Faulding Inc.*, 230 F.3d 1320 (Fed. Cir. 2000) (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1561 (Fed. Cir. 1991).

In both *Purdue Pharma* and *In re Ruschig*, the question of whether the specification provided support for the claimed invention arose under circumstances where the specification failed to provide literal support for particular limitations recited in the claims. In *Purdue Pharma*, claim 1 of the '360 patent described the compound for use in the claimed method as providing "a time to maximum plasma concentration (Tmax) of said opioid in about 2 to about 10 hours and a maximum plasma concentration (Cmax) which is more than twice the plasma level of said opioid at about 24 hours after administration of the dosage form." The question throughout the litigation was not whether the specification provided literal support for the recited

claim limitation, but rather, whether the specification provided implicit support for the recited claim limitation. The court recognized that satisfaction with the written description requirement does not require *in haec verba* support for the claimed subject matter, and focused the analysis on evaluating whether the specification allowed one skilled in the art to "immediately discern the limitation at issue in the claims." *Purdue Pharma L.P v. Faulding Inc.*, 230 F.3d at 1323-1324.

The court concluded that the alleged implicit support in the specification was not sufficient, and that the specification failed to adequately describe the recited claim limitation. "What the '360 patentees have done is to pick a characteristic possessed by two of their formulations, *a characteristic that is not discussed even in passing in the disclosure*, and then make it the basis of claims that cover not just those two formulations, but any formulation that has that characteristic." *Purdue Pharma L.P v. Faulding Inc.*, 230 F.3d at 1327 (emphasis added).

Similarly, in *In re Ruschig*, the question was whether the specification provided sufficient implicit support and guidance to support a claim directed to a single, specific chemical compound, despite the fact that the specification failed to explicitly recite the specific compound. Thus, the court's reference to "blaze marks" and "trees" in these cases occurs in a context where the specification fails to explicitly recite the particular claim limitations relied on for patentability.

In contrast, the instant specification explicitly recites all of the limitations of the claimed invention. For example, a SHH blocking antibody is specifically recited in, for example, paragraph [0029] of the published specification. Methods of inhibiting vascular growth in a variety of contexts (including cancer) are specifically recited in paragraphs [0060], [0096], [0107], and [0118] of the published specification. Further, the specification clearly reflects Applicants' understanding of the hedgehog signaling pathway, as well as an identification of compounds that agonize and antagonize hedgehog signaling and an appreciation that the SHH blocking antibody functioned as an antagonist. See, paragraphs [0078], [0089], [0093], [0095], and Example 4 of the published specification. Thus, unlike in *Purdue Pharma* and *In re Ruschig*, the question is not whether the instant specification provides implicit support for the claimed invention or whether one of skill in the art can "immediately discern the limitation at issue in the claims." Accordingly, Applicants submit that these cases do not support the New Matter rejection raised in the Advisory Action.

Applicants note that the distinction between whether claims are explicitly or implicitly supported by the specification, for the purpose of evaluating compliance with the written description requirement, is emphasized in the MPEP. See, MPEP 2163.05. Applicants draw the Examiner's attention to the MPEP merely to emphasize that Applicants are not distinguishing the instant application from the cited case law based on some inconsequential or minor point.

Applicants respectfully submit that the pending claims are fully compliant with the written description requirement and that Applicants' amendments do not add new matter. Unlike in *Purdue Pharma* and *In re Ruschig*, the instant specification provides more than mere blaze marks to the claimed invention. Rather, the instant specification provides explicit support for the claimed invention.

Issues Raised in the Office Action Mailed January 8, 2008

Information Disclosure Statement

Applicants note with appreciation that the Information Disclosure Statement of October 22, 2007 has been considered.

Withdrawn Objections and/or Rejections

Applicants note that the objections to the specification have been withdrawn.

Claim Rejection – 35 U.S.C. § 112, first paragraph, enablement

Claims 43, 57-60, 62-66, and 68 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

The basis of the rejection appears to be two-fold. First, as detailed on pages 3-5 of the instant Office Action, the Examiner alleges that Applicants' arguments and post-filing date evidence fail to support enablement of the claimed methods, as applied to the elected species of enhanced vascular growth accompanying a solid tumor. The Examiner alleges that the "relevant post-filing date art teaches variability in whether or not (and if so, how) the hedgehog pathway is activated in cancer." See, page 4 of the instant Office Action.

Applicants acknowledge that the post filing date art has revealed differing mechanisms by which hedgehog signaling may be misregulated in various types of cancers. Such

mechanisms include genetic alterations in tumor cells that lead to constitutive activation of the hedgehog pathway, as is observed in basal cell carcinoma and medullablastoma, as well as overexpression of hedgehog protein itself in tumors. As such, Applicants acknowledge that methods for modulating hedgehog signaling in cells harboring a mutation in a component of the hedgehog signaling pathway may require different compounds than methods for modulating hedgehog signaling in cells that overexpress hedgehog protein but do not harbor a mutation in a component of the hedgehog signaling pathway.

However, the claimed invention is not directed to modulating hedgehog signaling in tumor cells. Rather, the claimed invention is directed to inhibiting enhanced vascular growth, and the elected species is "enhanced vascular growth accompanying a solid tumor". The claims reflect an alternative approach to treating cancer by inhibiting the vascular growth required to feed the tumor. Such an approach is independent of whether the tumor itself is hedgehog dependent or hedgehog independent. In fact, since the early 1980s and Judah Folkman's pioneering work on the role of angiogenesis in facilitating tumor growth and metastasis, scientists have been investigating signaling pathways that can be modulated and compounds that can be used to treat cancer by inhibiting vascular growth. The appreciation that inhibition of the blood supply feeding a tumor can be used as a treatment is so generally accepted in the oncology field that the National Cancer Institute's website includes slides intended to explain this concept to the public. Exhibit 1 (a copy of which was previously provided with Applicants' response filed April 8, 2008).

The specification and post-filing art support a role for hedgehog signaling in vascular growth. Applicants enclose herewith complete copies of the Pola et al. articles referred to in Applicants' previous reply. Pola et al. (2001) Nature Medicine 7: 706-711 and Pola et al. (2003) Circulation 108: 479-85; copies of which were previously provided as Exhibits 2-3 of Applicants' response filed April 8, 2008. Applicants' evidence support the use of compounds that inhibit hedgehog signaling, for example a Sonic hedgehog blocking antibody, in methods for inhibiting vascular growth.

Regardless of whether the specification provides a working example of using a hedgehog compound in the context of a tumor, the pre- and post-filing art is replete with examples whereby angiogenesis is inhibited as part of a cancer treatment methodology. In fact, a search of the

clinical trials database maintained by the National Institutes of Health revealed over 1200 results based on the key word search "angiogenesis AND inhibitor AND tumor."

Applicants respectfully submit that the claimed methods, which are based on the use of compounds that inhibit vascular growth, are enabled independently of the cause of the underlying tumor (e.g., whether the underlying tumor is due to a mutation in or misexpression of a component of the hedgehog signaling pathway). The target of the claimed method is vascular growth that accompanies the tumor, and this target is generic to tumors of diverse etiology. Accordingly, Applicants submit that the claims are enabled throughout their scope.

The second basis of the Examiner's rejection, advanced on pages 6-7 of the instant Office Action, is that Applicants have allegedly failed to enable "a method of treatment using a genus of structurally undefined hedgehog signaling antagonists." See, page 6 of the instant Office Action. Applicants respectfully disagree. As detailed is Applicants' previous response, the specification and state of the art support the enablement of the claimed methods. Nevertheless, to expedite prosecution, Applicants have amended claim 43 (and claims depending therefrom) to more particularly point out that the compound for use in the claimed methods is a Sonic hedgehog blocking antibody. Applicants' amendments are not in acquiescence to any of the rejections raised during prosecution of this application. Applicants reserve the right to prosecute claims of similar or differing scope in this or future applications.

Additionally, Applicants have cancelled claims 57, 59, and 62-68 to avoid redundancy in view of Applicants' amendment to claim 43, as well as to expedite prosecution. Applicants reserve the right to prosecute claims of similar or differing scope in this or future applications. Applicants' cancellation of and amendments to the claims are believed to obviate the rejection.

The use of a Sonic hedgehog blocking antibody to inhibit vascular growth is supported by the working examples provided in the specification, as well as the post-filing date art of, for example, Pola et al. Furthermore, the state of the pre- and post-filing date art of cancer research supports the use of compounds that inhibit vascular growth to treat tumors. Accordingly, Applicants respectfully submit that the claims are enabled throughout their scope. Reconsideration and withdrawal of this rejection are requested.

Claim Rejection – 35 U.S.C. § 112, first paragraph, written description

Claim 43, 57-60, 62-66, and 68 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

Applicants reiterate the arguments of record and maintain that the specification provides ample support to evince that Applicants had possession of the claimed invention. In further support of Applicants' previous arguments that the factual situation in this case is distinguishable from the scenarios facing the court in *Vas-Cath*, *Fiers*, and *Amgen*, Applicants note that in *Capon v. Eshhar*, the Federal Circuit discussed in detail that the written description requirement must be analyzed in the context of the particular invention, technology, and state of the art ("the 'written description' requirement states that the patentee must describe the invention, it does not state that every invention must be described in the same way). *Capon v. Eshhar*, 418 F.3d 1349, 1358 (Fed. Cir. 2005). The claims at issue in *Capon* were directed to chimeric DNAs and expression vectors comprising the chimeric DNAs. Although the claims at issue in *Capon* were directed to biological compositions, the court still distinguished the factual situation from that of *Lilly*, *Fiers*, and *Amgen*. The court noted that in *Lilly*, *Fiers*, and *Amgen*, the claimed compositions included biological material that was unknown and had not been characterized. *Capon*, 418 F.3d at 1357-1358. In contrast, the compositions in *Capon*, although broadly and generically claimed without reference to particular sequences, were based on combining elements for which known examples existed in the art.

The factual situation in the instant case is more analogous to *Capon* than to *Lilly*, *Fiers*, and *Amgen*. Various hedgehog compounds, including nucleic acids, polypeptides, blocking antibodies, and small molecule inhibitors were already known in the art prior to Applicants' invention. Accordingly, Applicants' claims, which describe the use of such compounds, is unlike an attempt to claim an unknown biological material without reference to its specific sequence. In the present case, one of skill in the art can readily envision that which is claimed.

In the paragraph bridging pages 8 and 9, the Examiner provides an example of how *Lilly*, *Fiers*, and *Amgen* would be just as applicable to a method claim as to a composition claim. However, the example provided by the Examiner is one in which the compound itself was previously unknown. In contrast, the instant factual situation is more akin to *Capon*, where the art provided numerous examples of the biological compositions themselves. Accordingly, Applicants maintain that prevailing case law supports Applicants' position that the claims, prior

to Amendment, are fully compliant with the written description requirement.

The position articulated in *Capon* was followed by the Federal Circuit in *Falkner v. Inglis*. *Falkner v. Inglis*, 468 F.3d 1357, 1369 (Fed. Cir. 2006) ("As we stated in *Capon*, the 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way."). *Falkner* additionally held that

> "(1) examples are not necessary to support the adequacy of a written description; (2) the written description standard may be met (as it is here) even where actual reduction to practice of an invention is absent; and (3) there is no per se rule that an adequate written description of an invention that involves a biological macromolecule must contain a recitation of known structure."
> *Falkner*, 467 F.3d at 1367.

The foregoing arguments are equally applicable to claims reciting mean-plus-function language.

Nevertheless, to expedite prosecution, Applicants have amended claim 43 (and claims depending therefrom) to more particularly point out that the compound for use in the claimed methods is a Sonic hedgehog blocking antibody. Support for Applicants' amendment can be found, for example, in paragraphs [0029], [0089], and Example 4 of the published specification. Applicants' amendment is not in acquiescence to the rejection or to any of the arguments advanced by the Examiner during prosecution of the instant application. Applicants expressly reserve the right to prosecute claims of similar or differing scope.

Additionally, to expedite prosecution, Applicants have cancelled claims 57, 59, and 62-68. Cancellation of these claims is not in acquiescence to the rejection or to any of the arguments advanced by the Examiner during prosecution of the instant application. Applicants expressly reserve the right to prosecute claims of similar or differing scope. In view of Applicants' amendments, reconsideration and withdrawal of this rejection is requested. Applicants note that amended claim 43 is directed to the use of a Sonic hedgehog blocking antibody in the claimed methods. The Examiner indicated that claims directed to such subject matter satisfied the written description requirement. See, page 10 of the instant Office Action.

New Rejections

Claim Rejection – 35 U.S.C. § 112, first paragraph, written description (new matter)

Claims 43, 57-60, 62-66, and 68 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for allegedly containing new matter. Applicants traverse this rejection and contend that the rejection is moot in view of the amended claims.

Claim 43 (and claims depending therefrom) is rejected because the specification allegedly fails to support recitation of "a hedgehog antagonist capable of inhibiting hedgehog signaling." Applicants respectfully disagree with the Examiner's assessment and contend that, at the time of filing, one of skill in the art would have readily recognized that Applicants were in possession of methods for using a broad range of hedgehog compounds to inhibit abnormally enhanced vascular growth.

Nevertheless, to expedite prosecution, Applicants have amended claim 43 to more particularly point out that the compound for use in the claimed methods is a Sonic hedgehog blocking antibody. Support for Applicants' amendment can be found, for example, in paragraphs [0029], [0089], and Example 4 of the published specification. No new matter has been entered. Applicants note that a Sonic hedgehog blocking antibody (an antibody that binds to Sonic hedgehog protein to block its activity) was specifically used in the examples disclosed in the specification and is exemplary of a compound that inhibits hedgehog signaling.

Applicants' amendment is not in acquiescence to the rejection. Applicants expressly reserve the right to prosecute claims of similar or differing scope. Applicants' amendment is believed to obviate the rejection, and reconsideration and withdrawal of the rejection is requested.

Claim 57 is rejected because the specification allegedly lacks support for the genus of hedgehog antibodies that allegedly encompass antibodies against any component of the hedgehog pathway. Applicants traverse. Applicants note that claims 59, 62, and 63 depend from claim 57 and are rejected on the same basis.

Applicants contend that this rejection is based on the Examiner's unreasonably broad interpretation of the term "hedgehog antibody" as encompassing antibodies other than antibodies that bind to hedgehog protein. Nevertheless, to expedite prosecution and as detailed above, Applicants have amended claim 43 to point out that the compound for use in the claimed method is a Sonic hedgehog blocking antibody (an antibody that binds to Sonic hedgehog protein to

block its activity). In view of Applicants' amendment to claim 43, Applicants have cancelled claims 57, 59, 62, and 63 to avoid redundancy. Applicants expressly reserve the right to prosecute claims of similar or differing scope. Applicants' cancellation of claims 57, 59, 62, and 63 render this rejection moot, and withdrawal of this rejection is requested.

Claim 58 is rejected because the specification allegedly fails to support recitation of "a method of inhibiting angiogenesis." Applicants traverse. Applicants note that claims 59 and 65 are rejected on the same basis.

Applicants respectfully disagree with the Examiner's assessment. The specification repeatedly discusses vascular growth and methods for inhibiting vascular growth. Paragraph [0042] defines "vascular growth" as *at least one of* vasculogenesis and angiogenesis. (Emphasis added.). Applicants contend that this definition of vascular growth reflects the possession of modulating either or both vasculogenesis and angiogenesis. Accordingly, Applicants contend that claim 58 is fully supported by the specification.

Nevertheless, to expedite prosecution, Applicants have amended claim 58 to improve the clarity of the claim. Applicants' amendment is not in acquiescence to the rejection. Applicants' amendment is not believed to narrow the scope of the claim but, rather, is intended to improve the clarity of the claim. Applicants reserve the right to prosecute claims employing similar or differing language in this or future applications.

Claims 59 and 65 were rejected on the same grounds. Applicants have cancelled claim 59 to avoid redundancy in view of Applicants' amendment to claim 43. Applicants have cancelled claim 65 to expedite prosecution. Cancellation of claims 59 and 65 renders the rejection moot. Applicants expressly reserve the right to prosecute claims of similar or differing scope. In view of Applicants' amendment to claims 58, and in view of cancellation of claims 59 and 65, reconsideration and withdrawal of this rejection is requested.

Claim 60 is rejected because the specification allegedly fails to support recitation of "the enhanced vascular growth accompanies a tumor." Rather, the Examiner alleges that the specification supports methods for treating excess vascular growth found "in" a tumor. See, page 12 of the instant Office Action. Applicants traverse and contend that the rejection is moot in view of the amended claims. Applicants note that claims 62, 63, 66, and 68 are rejected on the same basis.

This rejection is based on the Examiner's unreasonably broad interpretation of the term "accompanying", as recited in the claims, and unreasonably narrow interpretation of the term "in", as recited in the specification. In contrast to the Examiner's interpretation, Applicants contend that, based on the knowledge in the art and the context of the specification and claims, the reasonable interpretation is that both terms refer to the same type of vascular growth that occurs *in the context of* cancer. For example, Applicants note that the word "in" is used in both paragraphs [0005] and [0118]. Paragraph [0005] describes the abnormal vascular growth observed *in* several conditions including tumors and rheumatoid arthritis. Clearly, the Examiner's narrow interpretation of "in" to refer to vascular growth within a tumor makes no sense when applied to rheumatoid arthritis. Rather, the reasonable interpretation of "in", as used in the specification is "in the context of". Applicants' recitation of "accompanying" was intended to capture this teaching of the specification.

Nevertheless, to expedite prosecution, Applicants have amended claim 60 to improve the clarity of the claims and to point out that, as supported by the specification, the claimed method is a method for treating a solid tumor. Applicants' amendment is not believed to narrow the scope of the claim but, rather, is intended to improve the clarity of the claim. Although claim 61 is withdrawn from consideration as directed to a nonelected species, Applicants have made a conforming amendment to claim 61. Applicants' amendment to claim 61 is believed to improve the clarity of the claim but is not believed to narrow its scope. Applicants' amendments are not in acquiescence to the rejection. Applicants reserve the right to prosecute claims employing similar or differing language in this or future applications.

Claims 62, 63, 66, and 68 were rejected on the same grounds. Applicants have cancelled claims 62 and 63 to avoid redundancy in view of Applicants' amendment to claim 43. Applicants have cancelled claims 66 and 68 to expedite prosecution. Cancellation of claims 62, 63, 66, and 68 renders the rejection moot. Applicants expressly reserve the right to prosecute claims of similar or differing scope. In view of Applicants' amendments to claims 60 and 61, and in view of cancellation of claims 62, 63, 66, and 68, reconsideration and withdrawal of this rejection is requested.

Claim 64 (and claims depending therefrom) is rejected because the specification allegedly fails to support recitation of "means for inhibiting hedgehog signaling." Applicants respectfully disagree with the Examiner's assessment and contend that, at the time of filing, one

of skill in the art would have readily recognized that antagonistic hedgehog compounds include a range of compounds that inhibit hedgehog signaling. Nevertheless, to expedite prosecution, Applicants have cancelled claim 64 (and claims depending therefrom). Cancellation of claims 64-68 is not in acquiescence to the rejection. Applicants expressly reserve the right to prosecute claims of similar or differing scope. Applicants' cancellation of claims 64-68 render the rejection moot, and withdrawal of this rejection is requested.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection. The pending claims are fully supported by the specification.

Claim Rejection – 35 U.S.C. § 112, second paragraph

Claims 64-66 and 68 are rejected under 35 U.S.C. 112, second paragraph, for allegedly failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants traverse this rejection.

The basis of the rejection is that the specification allegedly fails to set forth adequate disclosure to support the means plus function language recited in claims 64-68. Applicants respectfully disagree. Nevertheless, to expedite prosecution, Applicants have cancelled claims 64-66 and 68 (as well as claim 67 which was directed to a nonelected species). Cancellation of claims 64-68 is not in acquiescence of the rejection. Applicants expressly reserve the right to prosecute claims of similar or differing scope. Cancellation of claims 64-68 renders the rejection moot, and withdrawal of this rejection is requested.

Related Applications

The following co-pending applications have already been brought to the Examiner's attention and made of record during prosecution of this application: application serial number 10/727,195; application serial number 09/883,848; application serial number 10/652,686; application serial number 09/977,864; and application serial number 10/652,298. Prosecution in the co-pending applications is on going and Applicants invite the Examiner to consider prior or future prosecution in the co-pending applications.

The most recent action in application serial number 10/727,195 is an Advisory Action mailed May 12, 2008. The most recent action in application serial number 09/883,848 is a final Office Action mailed March 3, 2008. The most recent action in application serial number

10/652,686 is a Final Office Action mailed April 29, 2008. The most recent action in application serial number 09/977,864 is a reply and Request for Continued Examination mailed June 9, 2008 (responsive to a final Office Action mailed March 17, 2008). The most recent action in application serial number 10/652,298 is a reply and Request for Continued Examination mailed June 9, 2008 (responsive to a final Office Action mailed April 4, 2008).

CONCLUSION

If any clarification of the above response would facilitate prosecution of this application, Applicants respectfully request that the Examiner contact the undersigned at 617-951-7000. Should any further extension or other fee be required for timely consideration of this submission, Applicants hereby petition for same and request that the fee be charged to **Deposit Account No. 18-1945, under Order No. HUIP-P02-060**.

Respectfully Submitted,

Date: June 23, 2008

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